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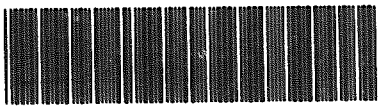
DuPont Central Research
and Development

FDCN: 88970000018

8EHQ-0197-13768

February 3, 1997

Via Federal Express


8EHQ-96-13768

Document Control Office (7407)
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street, SW
Washington, D.C. 20460

Contains No CBI

Re: 8EHQ-1096-13768

Dear Mr. Hernandez:

This letter is in response to your request for further information concerning the findings from a toxicity testing with the above referenced compound.

Enclosed is a copy of the final study report.

Sincerely,

A. Michael Kaplan, Ph.D.
Manager- Regulatory Affairs


89970000070

AMK:jat
(302)366-5260

Enclosure: Final Report, DuPont HLO-74-96, " Acute Inhalation Toxicity Study of HFC-236FA in Albino Rats".

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FINAL REPORT

STUDY TITLE

ACUTE INHALATION TOXICITY STUDY
OF HFC-236FA IN ALBINO RATS

STUDY DIRECTOR

Charles E. Ulrich, B.S.

STUDY INITIATED ON

March 7, 1996

STUDY COMPLETED ON

November 18, 1996

PERFORMING LABORATORY

WIL Research Laboratories, Inc.
1407 George Road
Ashland, OH 44805-9281

LABORATORY STUDY NUMBER

WIL-189022

SPONSOR

DuPont Fluoroproducts
P.O. Box 50
Newark, DE 19711

Acute Inhalation Toxicity Study
of HFC-236A in Albino Rats

COMPLIANCE STATEMENT

This study, designated WIL-189022, was conducted in compliance with the Organization for Economic Cooperation and Development (OECD) Principles of Good Laboratory Practice [C(81) 30 (Final) Annex 2], the Standard Operating Procedures of WIL Research Laboratories, Inc., and the protocol as approved by the sponsor.

C.E. Ulrich
Charles E. Ulrich, B.S.
Study Director

11-18-96
Date

Acute Inhalation Toxicity Study of HFC-236FA in Albino Rats

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Acute Inhalation Toxicity Study of HFC-236FA in Albino Rats

SUMMARY:

The acute inhalation toxicity of HFC-236FA was evaluated in this four-hour, single exposure study in five male and five female rats. The test article was administered via whole-body exposure as a vapor at a mean concentration of 457,000 parts per million (ppm). The exposure atmosphere was characterized by gas chromatography. Following the exposure, surviving animals were maintained for a 14-day observation period. Parameters evaluated were mortality, clinical observations, body weights and gross necropsy.

None of the rats died.

During the exposure, hyperactivity and then prostration were noted for all animals. At the one-hour post-exposure observation, there were no pharmacotoxic signs noted. All animals appeared normal on day 1 and for the remainder of the study. There were no other remarkable findings noted.

Two females exhibited slight body weight loss from day 0 to day 3 (less the 4% of day 0 weight). All rats appeared to have normal body weight by day 14 of the study.

Four animals had dark red lungs noted at necropsy. Two females had cysts on the kidneys and one female had an enlarged pituitary gland. There were no other findings at the scheduled necropsy.

Based on the data obtained from this study, the LC_{50} of HFC-236FA was found to be greater than 457,000 ppm when male and female rats were exposed to the material as a vapor for a single, four-hour period.

Acute Inhalation Toxicity Study of HFC-236FA in Albino Rats

INTRODUCTION:

The objective of this study was to determine the acute inhalation median lethal concentration (LC_{50}) and evaluate potential adverse effects of the test material when administered as a single, four-hour inhalation exposure to rats. The inhalation route was selected since inhalation was considered a potential route for human exposure to the test material.

The protocol was designed and the study was conducted in general compliance with the following guideline: Organization for Economic Cooperation and Development (OECD): Guideline No. 403, Acute Inhalation Toxicity, May 12, 1981.

Acute Inhalation Toxicity Study of HFC-236FA in Albino Rats

EXPERIMENTAL DESIGN:

This study consisted of one group of five male and five female albino rats. This group was exposed for four hours to a vapor concentration of the test material. Following the exposure, all survivors were maintained for a 14-day observation period. Body weights and observations for clinical signs were conducted periodically throughout the study. All animals underwent a gross necropsy.

The following table summarizes the experimental design;

Group Number	Target Exposure Concentration (ppm)
1	500,000

Experimental Start Date: April 3, 1996

Experimental Termination Date: April 17, 1996

MATERIALS AND METHODS:

Test System:

Species:	Rat
Strain:	Crl:CD®BR, Sprague-Dawley derived
Justification for Selection:	This species and strain of animal is recognized to be appropriate for acute inhalation studies.
Source:	Charles River Breeding Laboratories, Inc. 9801 Shaver Road Portage, MI 49081
Number on Study:	Five males and five females
Body Weight Range:	240 to 272 grams at initiation of exposure
Age at Start of Study:	Young adult
Method of Identification:	Ear tag
Housing:	Individual suspended wire-mesh cages. The animals were maintained by the animal husbandry staff of WIL Research Laboratories, Inc., in accordance with Standard Operating Procedures.
Quarantine:	The animals were acclimated to laboratory conditions for a minimum of seven days prior to initiation of exposure.
Food and Water:	Purina® Certified Rodent Chow® #5002 and tap water were provided *ad libitum* except during exposure when food and water were withheld. Analysis of feed was performed and provided by the manufacturer. Water was analyzed in accordance with Standard Operating Procedures. Contaminants were not present in feed or water at levels expected to interfere with the objectives of the study. Results of analyses are available upon Sponsor request.
Experimental Conditions:	Animal room with controlled temperature (71-73°F), humidity (24-54%) and light (12 hours light/12 hours dark).

Test Material Data:

Identification:	HFC-236FA
Source:	E.I. DuPont/Stine Haskell Elkton Road Newark, DE 19711
Date(s) Received:	March 8, 1996
Lot Number:	73550
Purity:	>99.5%
Stability:	Test material stability data are the responsibility of the Sponsor.
Physical Description:	Compressed gas in low-pressure cylinder
Storage Conditions:	Sealed container at ambient temperature
Test Material Preparation:	The test material was used as received from the Sponsor

Exposure Methods:

The exposure was conducted in a 110-L acrylic and glass exposure chamber. The animals were caged individually during the exposure.

Test Material Generation Methods:

Test material vapors were generated directly from the low pressure compressed gas cylinder using an appropriate regulator and flow meter. Compressed air for dilution was supplemented with pure oxygen (99%) at a rate sufficient to maintain an acceptable oxygen content level within the chamber.

Methods for Characterization of Exposure Atmospheres:

Nominal Concentrations:

Nominal exposure concentrations were calculated as the ratio of the test material gas flow divided by the total flow through the chamber which is the sum of the test material flow, compressed air flow and pure oxygen flow.

Actual Concentration:

Actual exposure concentrations were measured by injecting samples into a Hewlett-Packard 5890A Series II Gas Chromatograph (GC) with a 3396A integrator. Samples were collected in a 60-cc syringe through a septum port on the side of the chamber. Approximately 20 cc was withdrawn and transported to the GC where the entire volume was injected into the gas-sampling loop. The 0.25 ml volume of the loop was then automatically injected onto the column and subsequently to the detector.

The following table summarizes the gas chromatograph conditions:

Instrument:	Hewlett Packard 5890A Series II and a 3396A Integrator
Column:	Nine-meter X 1/8" OD stainless steel with 3% SP-1500 on Carbopack B, 80/120 mesh
Carrier:	Helium at approximately 19 ml/min
Column Temperature:	175°C, Isothermal
Detector:	Flame Ionization at 200°C
Injection Port Temperature:	250°C
Retention Time:	Approximately 1.9 minutes
Sampling Syringe:	60-cc BD plastic disposable

OBSERVATIONS:

Mortality:

The rats were observed during exposure and within one hour of removal from the exposure chamber/system on day 0 and twice daily thereafter for 14 days.

Clinical Observations:

The rats were observed during exposure and within one hour of removal from the exposure chamber/system on day 0 and once daily thereafter.

Body Weights:

Body weights were obtained immediately prior to exposure on day 0 and study days 3, 7 and 14.

Necropsy:

All animals were euthanized after the 14-day observation period and underwent a gross necropsy. Animals were euthanized by intravenous injection of sodium pentobarbital. The major organ systems of the cranial, thoracic and abdominal cavities were examined for all animals.

RESULTS:

Characterization of Exposure Atmospheres:

Environmental Conditions (Table 11):

Mean temperature and relative humidity of the exposure atmosphere are summarized in the following table:

Group Number	Temperature (°C) Mean	S.D.	N	Relative Humidity (%) Mean	S.D.	N	Oxygen (%) Mean	S.D.	N
1	25.5	4.57	12	42.0	9.16	12	21.5	5.33	12

Although the protocol specified an exposure chamber temperature of 20-24°C, the measured chamber temperature during exposure ranged from 19.7 to 30.8°C. There was no evidence that this deviation had any effect on the health of the animals. Therefore, this deviation was considered to have no impact on the scientific validity, integrity or outcome of the study.

Nominal Concentrations:

The following table summarizes the data used for determination of nominal exposure concentrations:

Group Number	TM Flow Rate (LPM)	Total Flow Rate (LPM)	Nominal Exposure Concentration (ppm)
1	8.8	18.7	471,000

While the protocol specified a chamber ventilation rate (CVR) of 12-15 air changes per hour (ACPH), only 10.2 ACPH were achieved. The 12-15 ACPH is so specified to ensure a sufficient amount of oxygen is present during non-oxygen-supplemented exposures. However, since oxygen was supplemented on this study and found to average 21.5%, the deviation from the protocol-specified CVR had no effect on the outcome of this study.

Actual Concentrations:

The following table summarizes the actual exposure concentration data:

Group Number	Mean Concentration (ppm)	Standard Deviation	Number of Samples
1	457,000	23,634	10

Mortality:

None of the rats on this study died.

Clinical Observations (Tables 1 and 5):

Shortly after initiation of exposure, all animals went through a brief period of hyperactivity before becoming prostrate. No other findings were noted during exposure.

There were no toxicologically significant observations noted at one hour post-exposure.

There were no toxicologically significant clinical observations noted during the 14-day post-exposure observation period.

Body Weights (Tables 2, 3, 6 and 7):

One female lost 9 grams and another lost 3 grams from day 0 to day 3. Both animals had surpassed their day 0 weight by day 14. There were no other remarkable body weight changes.

The following table summarizes the mean body weight data (grams) over the course of the study:

Sex	Group Number	Pre-Exposure	Study Day 3	Study Day 7	Study Day 14
Males	1	264	274	306	347
Females	1	249	249	254	258

Necropsy (Tables 4 and 8):

Four animals (1 male, 3 females) had dark red lungs noted at necropsy. Two females had cysts on the kidneys, and one female had an enlarged pituitary gland. There were no other findings at the scheduled necropsy.

CONCLUSIONS:

Based on the data obtained, the LC_{50} for HFC-236FA was found to be greater than 475,000 ppm when male and female albino rats were exposed for a single period of four hours under the conditions of this study.

PERSONNEL AND REPORT SUBMISSION:

Key Personnel: Robert R. Dahlgren, D.V.M., Ph.D., Diplomate A.C.V.P.
Director of Pathology and Veterinary Medicine

Kerin J. Clevidence, B.S.
Group Supervisor of Gross Pathology and
Developmental Toxicology Laboratory

Report Prepared By:

David W. Livingston, B.S.
Group Supervisor, Inhalation

11/18/96
Date

Report Reviewed By:

Bennett J. Varsho, B.S.
Manager of Inhalation Toxicology

11/18/96
Date

Approved and Submitted By:

Charles E. Ulrich, B.S.
Director of Inhalation

11-18-96
Date

QUALITY ASSURANCE UNIT STATEMENT:

Date(s) of Inspection(s)	Phase Inspected	Date(s) Findings Reported to Study Director	Date(s) Findings Reported to Management
4/10/96	Body Weights	4/10/96	5/28/96
6/27-28,7/1-2,19/96	Study Records (A-1)	7/19/96	8/26/96
6/27-28,7/1-2,19/96	Study Records (I-1)	7/19/96	8/26/96
6/27-28/7/1-2,19/96	Draft Report	7/19/96	8/26/96

This study was conducted and inspected in accordance with the Good Laboratory Practice Regulations, the Standard Operating Procedures of WIL Research Laboratories, Inc. and the protocol and protocol amendment(s), if any. Quality Assurance findings, derived from the inspection(s) during the conduct of the study and from the inspections of the raw data and draft report, are documented and have been reported to the Study Director. A status report is submitted to management monthly.

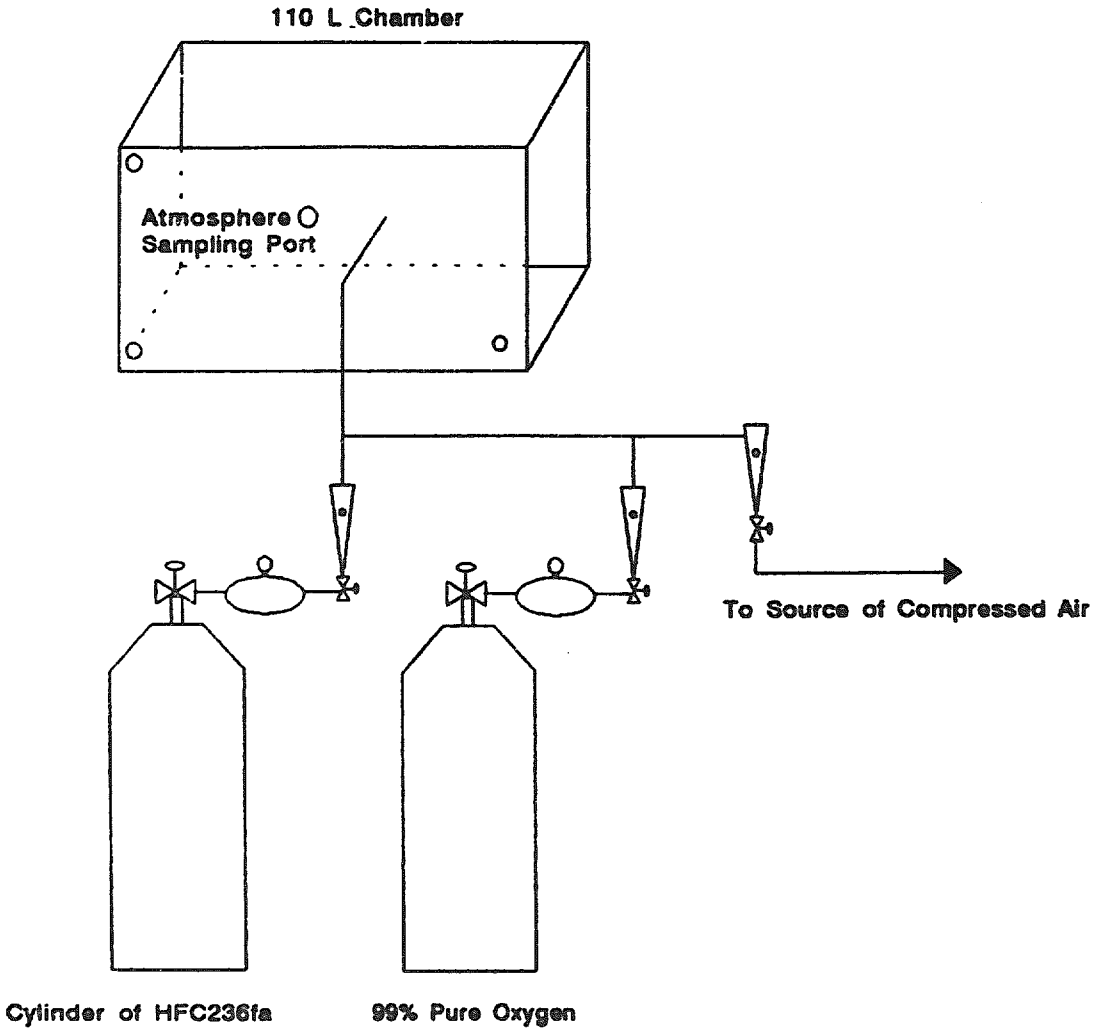
The raw data, the retention sample(s), if applicable, and the final report will be stored in the Archives at WIL Research Laboratories, Inc., or another location specified by the Sponsor.

Deborah L Little — 11/18/96

Deborah L. Little
Manager of Quality Assurance

Date

Figure I: Atmosphere Generation and Exposure System



Acute Inhalation Toxicity Study
of HFC-236FA in Albino Rats

Tables 1-11

TABLE 1

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
CLINICAL OBSERVATIONS SUMMARY OF INCIDENCE

----- M A L E -----

TABLE RANGE: DAY 0	
GROUP:	1
NUMBER IN DOSE GROUP	5
DURING EXPOSURE	
BEHAVIOR/CNS	
-HYPERACTIVITY	5
-PROSTRATE	5

TABLE 1

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
CLINICAL OBSERVATIONS SUMMARY OF INCIDENCE

----- F E M A L E -----

TABLE RANGE:	DAY 0	
GROUP:		1
NUMBER IN DOSE GROUP		5
	DURING EXPOSURE	
BEHAVIOR/CNS		
-HYPERACTIVITY		5
-PROSTRATE		5

TABLE 1
ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
CLINICAL OBSERVATIONS SUMMARY OF INCIDENCE

----- M A L E -----

TABLE RANGE: DAY 1 TO DAY 14	
GROUP:	1
NUMBER IN DOSE GROUP	5
NORMAL	
-NO SIGNIFICANT CLINICAL OBSERVATIONS	5
DISPOSITION	
-TERMINAL NECROPSY	5

TABLE 1
ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
CLINICAL OBSERVATIONS SUMMARY OF INCIDENCE

----- F E M A L E -----

	TABLE RANGE: DAY 1 TO DAY 14 GROUP: 1
NUMBER IN DOSE GROUP	5
NORMAL -NO SIGNIFICANT CLINICAL OBSERVATIONS	5
DISPOSITION -TERMINAL NECROPSY	5
EYES/EARS/NOSE -SCABBING- RIGHT EAR -SCABBING- LEFT EAR	 1 1

TABLE 2

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
BODY WEIGHTS (GRAMS) - SUMMARY OF MEANS

		----- MALE -----
	GROUP:	456,706 PPM
DAY 0		
	MEAN	264.
	S.D.	8.3
	N	5
3		
	MEAN	274.
	S.D.	7.5
	N	5
7		
	MEAN	306.
	S.D.	11.1
	N	5
14		
	MEAN	347.
	S.D.	15.8
	N	5

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

TABLE 2
ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
BODY WEIGHTS (GRAMS) - SUMMARY OF MEANS

		----- F E M A L E -----
	GROUP:	456,706 PPM
DAY 0		
	MEAN	249.
	S.D.	7.0
	N	5
3		
	MEAN	249.
	S.D.	4.8
	N	5
7		
	MEAN	254.
	S.D.	5.8
	N	5
14		
	MEAN	258.
	S.D.	5.9
	N	5

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

TABLE 3
ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

		----- M A L E -----
	GROUP:	456,706 PPM
DAY 0 TO 3		
	MEAN	11.
	S.D.	4.3
	N	5
3 TO 7		
	MEAN	31.
	S.D.	5.7
	N	5
7 TO 14		
	MEAN	41.
	S.D.	5.9
	N	5

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

TABLE 3
ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

		----- F E M A L E -----
GROUP:		456,706 PPM
DAY 0 TO 3		
	MEAN	0.
	S.D.	6.1
	N	5
3 TO 7		
	MEAN	5.
	S.D.	1.6
	N	5
7 TO 14		
	MEAN	4.
	S.D.	5.8
	N	5

TABLE 4

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
GROSS NECROPSY OBSERVATIONS INCIDENCE SUMMARY

SCHEDULED NECROPSY

	MALE	FEMALE
GROUP:	1	1
NUMBER OF ANIMALS IN DOSE GROUP	5	5
NUMBER OF ANIMALS TERMINALLY EUTHANIZED	5	5
KIDNEYS		
-CYST(S)	0	2
LUNGS		
-DARK RED AREA(S)	1	1
-DARK RED	0	2
PITUITARY		
-ENLARGED	0	1
NO SIGNIFICANT CHANGES OBSERVED - ALL EXAMINED TISSUES	4	1

1- 456,706 PPM

TABLE 5

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INCIDENCE AND SEVERITY OF CLINICAL OBSERVATIONS

DURING EXPOSURE

STUDY DAY : 0 OBSERVATION	SEX / DAY ANIMAL GROUP 0
HYPERACTIVITY	48577 M 1 P
	48578 M 1 P
	48579 M 1 P
	48583 M 1 P
	48585 M 1 P
	48588 F 1 P
	48591 F 1 P
	48592 F 1 P
	48594 F 1 P
	48595 F 1 P
PROSTRATE	48577 M 1 P
	48578 M 1 P
	48579 M 1 P
	48583 M 1 P
	48585 M 1 P
	48588 F 1 P
	48591 F 1 P
	48592 F 1 P
	48594 F 1 P
	48595 F 1 P

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE
SEX CODE: M = MALE F = FEMALE

TABLE 5

PROJECT NO.:WIL-189022 ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS PAGE 2
SPONSOR:DUPONT FLUOROPRODUCTS INCIDENCE AND SEVERITY OF CLINICAL OBSERVATIONS

STUDY DAY RANGE: 1 TO 14 OBSERVATION	ANIMAL	SEX / GROUP	DAY OF RANGE 1 2 3 4 5 6 7 8 9	10 11 12 13 14
NO SIGNIFICANT CLINICAL OBSERVATIONS	48577	M 1	P P P P P P P P P	P P P P
	48578	M 1	P P P P P P P P P	P P P P
	48579	M 1	P P P P P P P P P	P P P P
	48583	M 1	P P P P P P P P P	P P P P
	48585	M 1	P P P P P P P P P	P P P P
	48588	F 1	P P P P P P	
	48591	F 1	P P P P P P P P P	P P P P
	48592	F 1	P P P P P P P P P	P P P P
	48594	F 1	P P P P P P P P P	P P P P
	48595	F 1	P P P P P P P P P	P P P P
TERMINAL NECROPSY	48577	M 1		P
	48578	M 1		P
	48579	M 1		P
	48583	M 1		P
	48585	M 1		P
	48588	F 1		P
	48591	F 1		P
	48592	F 1		P
	48594	F 1		P
	48595	F 1		P
SCABBING- RIGHT EAR	48588	F 1	P P P P P P P P P	
SCABBING- LEFT EAR	48588	F 1	P P P	

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE
SEX CODE: M = MALE F = FEMALE

TABLE 6

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL BODY WEIGHTS (GRAMS)

MALE GROUP: 456,706 PPM

DAY	0	3	7	14
ANIMAL				
48577	272.	276.	301.	337.
48578	255.	270.	301.	341.
48579	264.	274.	313.	351.
48583	256.	266.	293.	332.
48585	272.	286.	321.	372.
MEAN	264.	274.	306.	347.
S.D.	8.3	7.5	11.1	15.8
N	5	5	5	5

TABLE 6

PROJECT NO.:WIL-189022 ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
SPONSOR:DUPONT FLUOROPRODUCTS INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALE GROUP: 456,706 PPM

DAY	0	3	7	14
ANIMAL				
48588	249.	252.	259.	254.
48591	240.	241.	244.	250.
48592	258.	249.	255.	264.
48594	254.	251.	255.	263.
48595	246.	253.	257.	258.
MEAN	249.	249.	254.	258.
S.D.	7.0	4.8	5.8	5.9
N	5	5	5	5

TABLE 7

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL BODY WEIGHT GAINS (GRAMS)

MALE GROUP: 456,706 PPM

DAY	0 TO 3	3 TO 7	7 TO 14
ANIMAL			
48577	4.	25.	36.
48578	15.	31.	40.
48579	10.	39.	38.
48583	10.	27.	39.
48585	14.	35.	51.
MEAN	11.	31.	41.
S.D.	4.3	5.7	5.9
N	5	5	5

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

TABLE 7
ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL BODY WEIGHT GAINS (GRAMS)

FEMALE GROUP: 456,706 PPM

DAY	0 TO 3	3 TO 7	7 TO 14
ANIMAL			
48588	3.	7.	-5.
48591	1.	3.	6.
48592	-9.	6.	9.
48594	-3.	4.	8.
48595	7.	4.	1.
MEAN	0.	5.	4.
S.D.	6.1	1.6	5.8
N	5	5	5

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

TABLE 8
ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL GROSS DESCRIPTION OF ORGANS

ANIMAL NO. 48577 GROUP 1: 456,706 PPM MALE SCHEDULED EUTH 04/17/96 DATE OF DEATH: 04/17/96 STUDY DAY: 14

	GRADE
NO SIGNIFICANT CHANGES OBSERVED	
GROSS: ADRENAL GLANDS	
BRAIN	
INTESTINE	
EPIDIDYMIDES	
ESOPHAGUS	
EYES	
HEART	
KIDNEYS	
LIVER	
LYMPH NODE, ME.	
LUNGS	
MAMMARY GLAND	
PANCREAS	
PITUITARY	
PROSTATE	
SALIVARY GLANDS	
SEMINAL VESICLES	
SKIN	
SPLEEN	
STOMACH	
TESTES	
THYMUS GLAND	
THYROID GLANDS	
TRACHEA	
URINARY BLADDER	

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

TABLE 8

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL GROSS DESCRIPTION OF ORGANS

ANIMAL NO. 48578 GROUP 1: 456,706 PPM MALE SCHEDULED EUTH 04/17/96 DATE OF DEATH: 04/17/96 STUDY DAY: 14

				GRADE
NO SIGNIFICANT CHANGES OBSERVED	GROSS: ADRENAL GLANDS	BRAIN	INTESTINE	EPIDIDYMIDES
	ESOPHAGUS	EYES	HEART	KIDNEYS
	LIVER	LYMPH NODE, ME.	LUNGS	MAMMARY GLAND
	PANCREAS	PITUITARY	PROSTATE	SALIVARY GLANDS
	SEMINAL VESICLES	SKIN	SPLEEN	STOMACH
	TESTES	THYMUS GLAND	THYROID GLANDS	TRACHEA
	URINARY BLADDER			

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

TABLE 8

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL GROSS DESCRIPTION OF ORGANS

ANIMAL NO. 48579 GROUP 1: 456,706 PPM MALE SCHEDULED EUTH 04/17/96 DATE OF DEATH: 04/17/96 STUDY DAY: 14

		GRADE
NO SIGNIFICANT CHANGES OBSERVED	GROSS:	

ADRENAL GLANDS	BRAIN	INTESTINE	EPIDIDYMIDES
ESOPHAGUS	EYES	HEART	KIDNEYS
LIVER	LYMPH NODE, ME.	LUNGS	MAMMARY GLAND
PANCREAS	PITUITARY	PROSTATE	SALIVARY GLANDS
SEMINAL VESICLES	SKIN	SPLEEN	STOMACH
TESTES	THYMUS GLAND	THYROID GLANDS	TRACHEA
URINARY BLADDER			

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

TABLE 8

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL GROSS DESCRIPTION OF ORGANS

ANIMAL NO. 48583 GROUP 1: 456,706 PPM MALE SCHEDULED EUTH 04/17/96 DATE OF DEATH: 04/17/96 STUDY DAY: 14

		GRADE
LUNGS	GROSS: DARK RED AREA(S) SEVERAL, 1 TO 3 MM IN DIAMETER, ALL LOBES	P
NO SIGNIFICANT CHANGES OBSERVED	GROSS:	

ADRENAL GLANDS	BRAIN	INTESTINE	EPIDIDYMIDES
ESOPHAGUS	EYES	HEART	KIDNEYS
LIVER	LYMPH NODE, ME.	MAMMARY GLAND	PANCREAS
PITUITARY	PROSTATE	SALIVARY GLANDS	SEMINAL VESICLES
SKIN	SPLEEN	STOMACH	TESTES
THYMUS GLAND	THYROID GLANDS	TRACHEA	URINARY BLADDER

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

TABLE 8

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL GROSS DESCRIPTION OF ORGANS

ANIMAL NO. 48585 GROUP 1: 456,706 PPM MALE SCHEDULED EUTH 04/17/96 DATE OF DEATH: 04/17/96 STUDY DAY: 14

				GRADE
NO SIGNIFICANT CHANGES OBSERVED	GROSS: ADRENAL GLANDS	BRAIN	INTESTINE	EPIDIDYMIDES
	ESOPHAGUS	EYES	HEART	KIDNEYS
	LIVER	LYMPH NODE, ME.	LUNGS	MAMMARY GLAND
	PANCREAS	PITUITARY	PROSTATE	SALIVARY GLANDS
	SEMINAL VESICLES	SKIN	SPLEEN	STOMACH
	TESTES	THYMUS GLAND	THYROID GLANDS	TRACHEA
	URINARY BLADDER			

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

TABLE 8

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL GROSS DESCRIPTION OF ORGANS

ANIMAL NO. 48588 GROUP 1: 456,706 PPM FEMALE SCHEDULED EUTH 04/17/96 DATE OF DEATH: 04/17/96 STUDY DAY: 14

		GRADE
LUNGS	GROSS: DARK RED AREA(S) SEVERAL, 1 TO 5 MM IN DIAMETER, ALL LOBES	P
NO SIGNIFICANT CHANGES OBSERVED	GROSS: ADRENAL GLANDS, BRAIN, INTESTINE, ESOPHAGUS, EYES, HEART, KIDNEYS, LIVER, LYMPH NODE, ME., MAMMARY GLAND, OVARIES, PANCREAS, PITUITARY, SALIVARY GLANDS, SKIN, SPLEEN, STOMACH, THYMUS GLAND, THYROID GLANDS, TRACHEA, URINARY BLADDER, UTERUS	

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

TABLE 8
ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL GROSS DESCRIPTION OF ORGANS

ANIMAL NO. 48591 GROUP 1: 456,706 PPM FEMALE SCHEDULED EUTH 04/17/96 DATE OF DEATH: 04/17/96 STUDY DAY: 14

		GRADE
PITUITARY	GROSS: ENLARGED	P
NO SIGNIFICANT CHANGES OBSERVED	GROSS:	

ADRENAL GLANDS	BRAIN	INTESTINE	ESOPHAGUS
EYES	HEART	KIDNEYS	LIVER
LYMPH NODE, ME.	LUNGS	MAMMARY GLAND	OVARIES
PANCREAS	SALIVARY GLANDS	SKIN	SPLEEN
STOMACH	THYMUS GLAND	THYROID GLANDS	TRACHEA
URINARY BLADDER	UTERUS		

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

TABLE 8
ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL GROSS DESCRIPTION OF ORGANS

ANIMAL NO. 48592 GROUP 1: 456,706 PPM FEMALE SCHEDULED EUTH 04/17/96 DATE OF DEATH: 04/17/96 STUDY DAY: 14

		GRADE
KIDNEYS	GROSS: CYST(S) ONE, 2 X 1 X 1 MM, LEFT	P
LUNGS	GROSS: DARK RED ALL LOBES	P
NO SIGNIFICANT CHANGES OBSERVED	GROSS: ADRENAL GLANDS, BRAIN, INTESTINE, ESOPHAGUS; EYES, HEART, LIVER, LYMPH NODE, ME.; MAMMARY GLAND, OVARIES, PANCREAS, PITUITARY; SALIVARY GLANDS, SKIN, SPLEEN, STOMACH; THYMUS GLAND, THYROID GLANDS, TRACHEA, URINARY BLADDER; UTERUS	

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

TABLE 8

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOX STUDY OF HFC-236FA IN RATS
INDIVIDUAL GROSS DESCRIPTION OF ORGANS

ANIMAL NO. 48594 GROUP 1: 456,706 PPM FEMALE SCHEDULED EUTH 04/17/96 DATE OF DEATH: 04/17/96 STUDY DAY: 14

		GRADE			
NO SIGNIFICANT CHANGES OBSERVED	GROSS: ADRENAL GLANDS	BRAIN	INTESTINE	ESOPHAGUS
	EYES	HEART	KIDNEYS	LIVER
	LYMPH NODE, ME.	LUNGS	MAMMARY GLAND	OVARIES
	PANCREAS	PITUITARY	SALIVARY GLANDS	SKIN
	SPLEEN	STOMACH	THYMUS GLAND	THYROID GLANDS
	TRACHEA	URINARY BLADDER	UTERUS	

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

ANIMAL NO. 48595 GROUP 1: 456,706 PPM FEMALE SCHEDULED EUTH 04/17/96 DATE OF DEATH: 04/17/96 STUDY DAY: 14

			GRADE
	KIDNEYS	GROSS: CYST(S) ONE, 2 MM IN DIAMETER, LEFT	P
	LUNGS	GROSS: DARK RED ALL LOBES	P
	NO SIGNIFICANT CHANGES OBSERVED	GROSS: ADRENAL GLANDS, BRAIN, INTESTINE, ESOPHAGUS, EYES, HEART, LIVER, LYMPH NODE, ME., MAMMARY GLAND, OVARIES, PANCREAS, PITUITARY, SALIVARY GLANDS, SKIN, SPLEEN, STOMACH, THYMUS GLAND, THYROID GLANDS, TRACHEA, URINARY BLADDER, UTERUS	

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT

TABLE 9

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOXICITY STUDY OF HFC-236FA IN ALBINO RATS
GAS CHROMATOGRAPH CALIBRATION DATA

DATE OF CALIBRATION: 4/2/96

STANDARD PREPARED	AREA	AMT/AREA	MEAN AMT/AREA	S.D.	C.V.(%)
250,000					
TRIAL 1	10898656	2.2939E-02			
TRIAL 2	11003808	2.2719E-02	2.2819E-02	1.1127E-04	0.49
TRIAL 3	10964760	2.2800E-02			
500,000					
TRIAL 1	21596688	2.3152E-02			
TRIAL 2	21659040	2.3085E-02	2.3070E-02	8.9902E-05	0.39
TRIAL 3	21763568	2.2974E-02			
750,000					
TRIAL 1	32793168	2.2871E-02			
TRIAL 2	32991136	2.2733E-02	2.2847E-02	1.0410E-04	0.46
TRIAL 3	32698160	2.2937E-02			
		MEAN:	2.2912E-02		
		S.D.:	1.3755E-04		
		CV(%):	0.60		

STANDARD CONCENTRATION IN: PARTS PER MILLION

TABLE 10

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOXICITY STUDY OF HFC-236FA IN ALBINO RATS
INDIVIDUAL SAMPLE CONCENTRATION DATA

CONCENTRATIONS FOR STUDY DAY: 0 EXPOSURE DATE: 4-3-96

GROUP: 1

	CH. NO. 1 ACUTE CONC.
00:10	402,544
00:30	475,299
01:00	457,980
01:30	456,110
02:00	478,752
02:30	489,444
02:45	457,518
03:00	447,644
03:30	455,199
04:00	446,565
MEAN	456,706
SD	23,634
CV(%)	5.17
N	10

CH. = CHAMBER, NO. = NUMBER, CONC. = CONCENTRATION
CONCENTRATION IN: PARTS PER MILLION

TABLE 11

PROJECT NO.:WIL-189022
SPONSOR:DUPONT FLUOROPRODUCTS

ACUTE INHALATION TOXICITY STUDY OF HFC-236FA IN ALBINO RATS
CHAMBER ENVIRONMENTAL CONDITIONS

TIME (HH:MM)	TEMPERATURE (°C)	RELATIVE HUMIDITY (%)	OXYGEN CONTENT (%)
00:20	19.7	67.5	22.3
00:40	20.1	51.7	21.3
01:00	20.1	44.4	22.2
01:20	20.4	40.6	21.3
01:40	23.5	38.8	22.0
02:00	25.3	38.1	20.8
02:20	27.0	36.9	21.4
02:40	28.4	37.5	21.6
03:00	29.4	36.9	20.9
03:20	30.1	36.3	20.6
03:40	31.2	37.5	21.6
04:00	30.8	37.5	21.4
MEAN	25.5	42.0	21.5
SD	4.57	9.16	5.33
CV(%)	17.92	21.81	24.79
N	12	12	12

Acute Inhalation Toxicity Study
of HFC-236FA in Albino Rats

APPENDIX A

Protocol and Protocol Amendments

Study Number: WIL-189022

PROTOCOL AMENDMENT I

Sponsor: E. I. du Pont de Nemours and Company

A. Title of Study:

Acute Inhalation Toxicity Study of HFC-236FA in Albino Rats

B. Protocol Modification:

1) III. STUDY SCHEDULE DATA

A. Proposed Experimental Start Date: April 3, 1996

B. Proposed Experimental Termination Date: April 17, 1996

C. Proposed Audited Draft Report Date: July 31, 1996

C. Reason for Protocol Modification:

1) To update study schedule data.

Approved By:

DuPont Fluoroproducts
P.O. Box 50
Newark, DE 19714

William J. Brock, Ph.D.
Sponsor Representative

8-6-96
Date

Prepared By:

WIL Research Laboratories, Inc.
Ashland, OH 44805-9281

C.E. Ulrich

Charles E. Ulrich, B.S.
Study Director

8-1-96
Date

PROTOCOL

Acute Inhalation Toxicity Study of HFC-236FA in Albino Rats

(OECD Guidelines)

Study No.: WIL-189022

For

DuPont Fluoroproducts
P.O. Box 50
Newark, DE 19711

By

WIL Research Laboratories, Inc.
Ashland, OH 44805-9281

March 7, 1996

WIL Study No.: WIL-189022

I. OBJECTIVE OF STUDY

To determine the acute inhalation median lethal concentration (LC_{50}) and evaluate potential adverse effects of the test material when administered as a single, four-hour inhalation exposure to rats.

This protocol has been designed and the study will be conducted in compliance with the Organization for Economic Cooperation and Development (OECD) Guidelines for Testing of Chemicals, Section 403.

II. PERSONNEL INVOLVED IN THE STUDY

A. Sponsor Representative

William J. Brock, Ph.D.
Study Monitor

B. WIL Study Director

Charles E. Ulrich, B.S.
Director of Inhalation Toxicology

C. Deputy Director

Christopher P. Chengelis, Ph.D., D.A.B.T.
Senior Toxicologist

D. WIL Toxicology Department Responsibilities

1. James L. Schardein, M.S., A.T.S.
   Director of Research

2. Loren W. Severs, M.S.
   Manager of Analytical Chemistry

3. Ronald E. Wilson, B.S.
   Director of Informational Systems

4. John F. Knapp, B.S.
   Manager of Pharmacy

5. Sally A. Keets, A.S.
   Manager of Vivarium

II. PERSONNEL INVOLVED IN THE STUDY (continued)

6. Deborah L. Little
   Manager of Quality Assurance

7. Kerin Clevidence, B.S.
   Group Supervisor - Necropsy

8. Robert R. Dahlgren, D.V.M., Ph.D., Diplomate A.C.V.P.
   Director of Pathology and Veterinary Medicine

9. David W. Livingston, B.S.
   Group Supervisor - Inhalation

III. STUDY SCHEDULE DATA

A. Proposed Experimental Start Date: To be added by protocol amendment.

B. Proposed Experimental Termination Date: To be added by protocol amendment.

C. Proposed Audited Draft Report Date: To be added by protocol amendment.

IV. TEST MATERIAL DATA

A.	Identification:	HFC-236FA
B.	Lot Number:	To be provided by Sponsor.
C.	Purity:	To be provided by Sponsor.
D.	Stability:	To be provided by Sponsor.
E.	Physical Description:	To be documented by WIL Research Laboratories, Inc.
F.	Storage Conditions:	To be provided by Sponsor.
G.	Personnel Safety Data:	See attached Material Safety Data Sheet.

V. TEST SYSTEM

A.	Species:	Rat
B.	Strain:	Crl:CD®BR, Spraque-Dawley derived

V. TEST SYSTEM (continued)

C. Source: The Charles River Breeding Laboratories, Inc.
9801 Shaver Road
Portage, MI 49081

D. Number on Study: Minimum required to establish LC_{50}; five males and five females per group.

E. Approximate Weight: 200 to 300 grams at initiation of exposure, ± 20% of the mean for each sex.

F. Approximate Age: Young adult

G. Identification System: Animals will be uniquely identified by a metal eartag displaying the animal number. Individual cage cards will be affixed to each cage and will display the study number, group (exposure level), animal number, sex and the dates of animal arrival and initiation of exposure.

H. Justification for Selection: This species and strain is generally recognized to be appropriate for acute inhalation studies.

VI. SPECIFIC (NONEXPOSURE PERIOD) MAINTENANCE SCHEDULE

A. Animal Housing

The animals will be individually housed in suspended wire-mesh cages in an environmentally controlled room. The cages will be elevated above cage-board or other suitable material which will be changed at least three times each week. The cages will be subject to routine cleaning at a frequency consistent with maintaining good animal health.

B. Environmental Conditions

Controls will be set to maintain temperature at 72° ± 4°F and relative humidity at approximately 30-70%. Fluorescent lighting controlled by light timers will provide illumination for a 12-hour light/dark photoperiod. Temperature and relative humidity will be recorded once daily.

VI. SPECIFIC (NONEXPOSURE PERIOD) MAINTENANCE SCHEDULE (continued)

C. Drinking Water

Municipal tap water will be available *ad libitum*. Filters servicing the automatic watering system are changed regularly according to Standard Operating Procedures. Water supplying the laboratory is analyzed for contaminants according to Standard Operating Procedures to ascertain that none are present at concentration that would be expected to affect the outcome of the study.

D. Basal Diet

Purina® Certified Rodent Chow® #5002 will be offered *ad libitum* during the study. Periodic analyses of the certified feed for the presence of heavy metals and pesticides are performed and provided by the manufacturer to ensure that none are present at concentrations that would be expected to affect the outcome of the study.

VII. EXPERIMENTAL DESIGN

A. Animal Receipt and Quarantine

Each animal will be inspected by a qualified technician upon receipt. Animals judged to be in good health and suitable as test subjects will be placed immediately in quarantine for a minimum of seven days. All animals will be sexed, weighed and permanently identified with an eartag.

During the quarantine period, each animal will be observed twice daily for changes in general appearance and behavior. Prior to initiation of exposure, those animals judged to be suitable test subjects will be identified.

B. Randomization

Animals will be ordered specifically for this study or selected from a colony maintained for acute studies. The animals will be selected based on the body weight requirements and on the appearance of general good health.

Formal randomization will not be required when only one exposure is to be conducted on a given day. However, when more than one exposure is to be conducted on a given day, then the animals selected based on body weight and appearance of good health will be formally randomized, using simple randomization, into the requisite groups.

VII. EXPERIMENTAL DESIGN (continued)

C. Exposure Levels and Treatment Regimen

1. Exposure Levels

A minimum of three exposure levels is recommended to establish a defined inhalation LC_{50}. These levels may be selected based on range-finding study results or in a progression utilizing the 5.0 mg/L (825 ppm) level as one of the levels in the defined LC_{50} study. In either case, a total of three levels (minimum) will be conducted for determination of a definitive LC_{50}.

Five males and five females per treatment group will be employed unless specified otherwise by the Sponsor.

2. Treatment Regimen

Animals will be exposed to the test atmosphere for a single, four-hour period.

D. Route and Rationale of Test Material Administration

The route of administration will be whole-body inhalation exposure since this is the anticipated route of human exposure.

E. Exposure Methods

Exposures will be conducted in all glass or stainless-steel and glass whole-body exposure chambers. The chambers will be operated under dynamic conditions where the chamber ventilation air is supplied either from a HEPA and charcoal filtered air source, from filtered room air or from an in-house compressed air source.

Air flow rate through the chamber will be such that there will be at least 12 air changes per hour. Average chamber temperature and relative humidity will be 22±2°C and 40-70%, respectively. These parameters will be monitored continuously and recorded at approximately 20-minute intervals during each exposure. Oxygen content of the exposure atmosphere will be measured during the methods development phase of the study and will be at least 19%.

All animals will be caged individually during the exposure. Food and water will not be available during the exposures.

VII. EXPERIMENTAL DESIGN (continued)

F. Test Material Generation Methods

The test material will be generated as a vapor atmosphere. Details of generation system methodologies cannot be defined until the exposure levels are defined and the physical and chemical characteristics of the test material are known. Therefore, this information will be recorded in the data records after preliminary methods evaluations are conducted.

G. Methods of Characterization of Exposure Atmospheres

1. Nominal Concentrations

Nominal exposure concentrations will be calculated for all exposures.

2. Actual Exposure Concentrations

Exposure concentrations will be measured by an appropriate analytical method (gas chromatography, total hydrocarbon analyzer or gas phase infra-red analyzer). All results will be evaluated in terms of the actual measured concentrations. At least four (4) determinations will be made during each exposure.

3. Aerosol Particle Size Determination

Aerosol particle size determination will not be required for this study.

VIII. EXPERIMENTAL OBSERVATIONS

A. Viability and Clinical Observations

During the exposure, those animals visible through the chamber windows will be observed for pharmacotoxic signs and mortality at least once, approximately midway through the exposure. All animals will be observed for mortality and pharmacotoxic signs on removal from the exposure system. The animals will be observed daily thereafter for 14 days for pharmacotoxic signs and twice daily (morning and afternoon) for mortality. If signs are present at the end of 14 days of observations that may be related to the test material, then the observation period may be extended until such signs are no longer present or are obviously irreversible (additional cost will be incurred).

B. Body Weights

The body weight of each animal will be determined immediately prior to exposure on day 0, and on days 3, 7 and 14 (termination). In addition, animals that die on study will be weighed.

IX. GROSS PATHOLOGY

At study termination, surviving animals will be euthanized by intravenous injection of sodium pentobarbital solution. A gross necropsy examination on major organ systems of the cranial, thoracic and abdominal cavities will be conducted on all animals found dead or at termination.

X. DETERMINATION OF LC_{50}

At the termination of the project, all data will be collected and the acute inhalation toxicity of the test material will be determined by an appropriate method. If possible, an LC_{50} value with 95% confidence limits will be calculated by the method of Litchfield and Wilcoxon.

XI. REPORT

The final report will include the following: summary, objective, test material identification and receipt, method of test atmosphere generation and characterization, observations, mortality, body weights, gross necropsy findings and an estimated or calculated LC_{50}. Two copies of the final report will be provided approximately ten weeks following completion of the study.

XII. QUALITY ASSURANCE

The study will be audited by the WIL Quality Assurance Unit while in progress to assure compliance with OECD Good Laboratory Practice Regulations, adherence to the protocol and to WIL Standard Operating Procedures. The raw data and draft report will be audited by the WIL Quality Assurance Unit prior to submission to the Sponsor to assure that the final report accurately describes the conduct and the findings of the study.

XIII. RECORDS TO BE MAINTAINED

All original raw data, as defined by WIL SOPs and the applicable GLPs, will be maintained in permanently bound notebooks or in loose-leaf notebooks and at study completion will be stored in the Archives at WIL Research Laboratories, Inc.

XIV. WORK PRODUCT

Sponsor will have title to all documentation records, raw data, slides, specimens, or other work product generated during the performance of the study. All work product including raw paper data, magnetically encoded records and specimens will be retained at no charge for a period of six months following issuance of the final report in the Archives at WIL Research Laboratories, Inc. Thereafter, WIL Research Laboratories will charge a monthly archiving fee for retention of all work product. All work product will be stored in compliance with regulatory requirements.

XV. PROTOCOL MODIFICATION

Modification of the protocol may be accomplished during the course of this investigation. However, no changes will be made in the study design without the verbal or written permission of the Sponsor. In the event that the Sponsor verbally requests or approves a change in the protocol, such changes will be made by appropriate documentation in the form of a protocol amendment. All alterations of the protocol and reasons for the modification(s) will be signed by the Study Director and the Sponsor Representative.

XVI. ANIMAL WELFARE ACT COMPLIANCE

This study will comply with all applicable sections of the Final Rules of the Animal Welfare Act regulations (9 CFR). The Sponsor should make particular note of the following:

1. The Sponsor signature on this protocol documents for the Study Director the Sponsor's assurance that the study described in this protocol does not unnecessarily duplicate previous experiments.

2. Whenever possible, procedures used in this study have been designed to avoid or minimize discomfort, distress or pain to animals. All methods are described in this study protocol or in written laboratory Standard Operating Procedures.

3. Animals that experience severe or chronic pain or distress that cannot be relieved will be painlessly euthanized as deemed appropriate by the veterinary staff and Study Director. The Sponsor will be advised by the Study Director of all circumstances which could lead to this action in as timely a manner as possible.

4. Methods of euthanasia used during this study are in conformance with the above-referenced regulation.

XVII. PROTOCOL APPROVAL

DuPont Fluoroproducts
P.O. Box 50
Newark, DE 19711

William J. Brock, Ph.D.
Sponsor Representative

March 20, 1996
Date

WIL Research Laboratories, Inc.
Ashland, OH 44805-9281

C.E. Ulrich
Charles E. Ulrich, B.S.
Study Director

Mar. 7 96
Date

6095FR | HFC-236fa | Revised 4-AUG-1995 | Printed 20-MAR-1996

CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Material Identification

CAS Number : 690-39-1
Formula : CF3-CH2-CF3
CAS Name : 1,1,1,3,3,3-hexafluoropropane

Tradenames and Synonyms

HEXAFLUOROPROPANE
CC0610

Company Identification

MANUFACTURER/DISTRIBUTOR
DuPont
1007 Market Street
Wilmington, DE 19898

PHONE NUMBERS
Product Information : 1-800-441-7515
Transport Emergency : CHEMTREC 1-800-424-9300
Medical Emergency : 1-800-441-3637

COMPOSITION/INFORMATION ON INGREDIENTS

Components

Material	CAS Number	%
1,1,1,3,3,3-HEXAFLUOROPROPANE	690-39-1	99-100

HAZARDS IDENTIFICATION

Potential Health Effects

INHALATION

1,1,1,3,3,3-HEXAFLUOROPROPANE
Based on animal data, this material may cause: Suffocation, if air is displaced by vapors. Irregular heart beat with a strange sensation in the chest, "heart thumping", apprehension, lightheadedness, feeling of fainting, dizziness, weakness, sometimes progressing to loss of consciousness and death.

SKIN CONTACT

1,1,1,3,3,3-HEXAFLUOROPROPANE
Frostbite, if liquid or escaping vapor contacts the skin.

(HAZARDS IDENTIFICATION - Continued)

EYE CONTACT

1,1,1,3,3,3-HEXAFLUOROPROPANE
"Frostbite-like" effects may occur if the liquid or escaping vapors contact the eyes.

INGESTION

1,1,1,3,3,3-HEXAFLUOROPROPANE
Not a probable route of exposure.

Carcinogenicity Information

None of the components present in this material at concentrations equal to or greater than 0.1% are listed by IARC, NTP, OSHA or ACGIH as a carcinogen.

FIRST AID MEASURES

First Aid

INHALATION

If inhaled, immediately remove to fresh air. Keep person calm. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Call a physician.

SKIN CONTACT

Flush area with lukewarm water. Do not use hot water. If frostbite has occurred, call a physician.

EYE CONTACT

In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Call a physician.

INGESTION

Ingestion is not considered a potential route of exposure.

FIRE FIGHTING MEASURES

Flammable Properties

Will not burn. Not a fire or explosion hazard.

Hazardous gases/vapors produced in fire are hydrogen fluoride.

(FIRE FIGHTING MEASURES - Continued)

Extinguishing Media

Use media appropriate for surrounding material.

Fire Fighting Instructions

Wear self-contained breathing apparatus. Wear full protective equipment. Cool tank/container with water spray.

ACCIDENTAL RELEASE MEASURES

Safeguards (Personnel)

NOTE: Review FIRE FIGHTING MEASURES and HANDLING (PERSONNEL) sections before proceeding with clean-up. Use appropriate PERSONAL PROTECTIVE EQUIPMENT during clean-up.

Keep upwind of leak - evacuate until gas has dispersed.

Accidental Release Measures

Ventilate area before reentering.

HANDLING AND STORAGE

Handling (Personnel)

Do not breathe gas. Do not get in eyes, on skin, or on clothing. Wash thoroughly after handling.

Handling (Physical Aspects)

Keep away from heat, sparks and flames.

Storage

Keep container in a cool place. Keep container tightly closed.

EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls

Use only with adequate ventilation. Keep container tightly closed.

Vapors of the compound are heavier than air, posing a hazard of asphyxia if they are trapped in enclosed or low places.

Personal Protective Equipment

EYE/FACE PROTECTION

(EXPOSURE CONTROLS/PERSONAL PROTECTION - Continued)

Wear safety glasses or coverall chemical splash goggles.

RESPIRATORS

Wear NIOSH/MSHA approved respiratory protection, as appropriate.

PROTECTIVE CLOTHING

Wear impervious clothing, such as gloves, apron, boots, or whole bodysuit as appropriate.

Exposure Guidelines

Exposure Limits
HFC-236fa

PEL	(OSHA)	: None Established
TLV	(ACGIH)	: None Established
AEL *	(DuPont)	: 1000 ppm, 8 & 12 Hr. TWA

* AEL is DuPont's Acceptable Exposure Limit. Where governmentally imposed occupational exposure limits which are lower than the AEL are in effect, such limits shall take precedence.

PHYSICAL AND CHEMICAL PROPERTIES

Physical Data

Boiling Point	: -.7 C (30.7 F)
Vapor Pressure	: 36 psia @ 25 C (calc'd)
Melting Point	: -93.6 C (-136.5 F)
Freezing Point	: -96.3 C (-141.3 F)
Form	: Liquefied gas
Color	: Colorless
Specific Gravity	: 1.370 gm/cc

STABILITY AND REACTIVITY

Incompatibility with Other Materials

Incompatible with Strong bases, metallic sodium, potassium, lithium.

Decomposition

Decomposes with heat.

Hazardous gases/vapors produced are hydrogen fluoride.

Polymerization

Polymerization will not occur.

TOXICOLOGICAL INFORMATION

Animal Data

INHALATION:

4 hour, ALC, rat: > 189,000 ppm.

Single exposure caused: Narcosis. Cardiac sensitization, a potentially fatal disturbance of heart rhythm associated with a heightened sensitivity to the action of epinephrine. Repeated exposure caused: No significant toxicological effects. No-Observed-Adverse-Effect-Level (NOAEL): 20,000 ppm.

CARCINOGENIC, DEVELOPMENTAL, REPRODUCTIVE, MUTAGENIC EFFECTS:

Limited studies do not suggest developmental toxicity. Specific studies to evaluate the effect on female reproductive performance have not been conducted; however, limited information obtained from studies on developmental toxicity do not indicate adverse effects on female reproductive performance. Tests have shown that this material does not cause genetic damage in bacterial or mammalian cell cultures. No animal data are available to define the following effects of this material: carcinogenicity.

DISPOSAL CONSIDERATIONS

Waste Disposal

Treatment, storage, transportation, and disposal must be in accordance with applicable Federal, State/Provincial, and Local regulations.

TRANSPORTATION INFORMATION

Shipping Information

NOT REGULATED AS A HAZARDOUS MATERIAL BY DOT, IMO, OR IATA.

OTHER INFORMATION

NFPA, NPCA-HMIS

NPCA-HMIS Rating

Health	: 1
Flammability	: 0
Reactivity	: 1

Additional Information

Not listed on the TSCA Public inventory. If absent from the Master inventory use only for applications excluded or exempted from TSCA.

The data in this Material Safety Data Sheet relates only to the specific material designated herein and does not relate to use in combination with any other material or in any process.

Responsibility for MSDS	: DuPont Chemicals
Address	: Engineering & Product Safety
>	: P.O. Box 80709, Chestnut Run
>	: Wilmington, DE 19880-0709
Telephone	: (302) 999-4946

# Indicates updated section.

End of MSDS